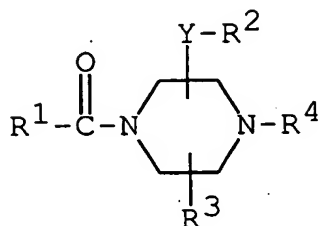


## C L A I M S

1. A compound of the formula :



wherein

Y is bond or lower alkylene,

R<sup>1</sup> is aryl which may have substituent(s),

R<sup>2</sup> is aryl or indolyl, each of which may have substituent(s),

R<sup>3</sup> is hydrogen or lower alkyl;

R<sup>4</sup> is pyridyl(lower)alkylamino(lower)alkynyl;

N-(lower alkyl)-N-[pyridyl(lower)alkyl]amino-(lower)alkyl;

hydroxy(lower)alkoxy(lower)alkyl;

lower alkanoyl(lower)alkoxy(lower)alkyl;

phenyl(lower)alkyl which has hydroxy(lower)alkyl or morpholinyl(lower)alkyl;

ar(lower)alkoxycarbonyl;

(2-pyridyl)(lower)alkyl which may have 1 to 3 substituent(s) selected from the group consisting of lower alkyl, lower alkoxy, lower alkoxycarbonyl, mono(or di or tri)halo(lower)alkyl and halogen;

(3-pyridyl)propyl which may have lower alkoxy or amino;

(3-pyridyl)butyl which may have lower alkoxy or amino;

pyridyl(lower)alkenyl which may have lower alkoxy or amino;

(2-pyridyl)(lower)alkynyl which may have 1 to 3

substituent(s) selected from the group consisting of lower alkyl, lower alkoxy, lower alkoxycarbonyl, mono(or di or tri)halo(lower)alkyl and halogen; (3-pyridyl)(lower)alkynyl which may have lower

5

alkoxy or amino;

pyridyl, thiazolyl, imidazolyl or pyrazolyl, each of which may have substituent(s);

imidazolyl(lower)alkyl which may have 1 or 2

10

substituent(s) selected from the group consisting of lower alkyl, lower alkynyl, ar(lower)alkyl, pyridyl(lower)alkyl, mono(or di or tri)halo(lower)alkyl and halogen;

pyrazolyl(lower)alkyl which may have

15

hydroxy(lower)alkyl, carboxy(lower)alkyl, lower alkoxycarbonyl(lower)alkyl, morpholinyl(lower)alkyl or morpholinylcarbonyl(lower)alkyl;

thiazolyl(lower)alkyl which may have lower alkyl;

piperidyl(lower)alkyl which may have

hydroxy(lower)alkyl or lower alkoxy;

20

morpholinyl(lower)alkyl which has 1 or 2

substituent(s) selected from the group consisting of ethyl, hydroxy(lower)alkyl, halo(lower)alkyl and lower alkoxy(lower)alkyl;

morpholinyl(lower)alkyl which has lower alkyl and lower alkoxy(lower)alkyl;

25

(3,5-dimethylmorpholino)(lower)alkyl;

morpholino(lower)alkenyl which may have lower alkyl or lower alkoxy(lower)alkyl;

(2- or 3-morpholinyl)(lower)alkenyl which may have lower alkoxycarbonyl;

30

pyrrolidinyl(lower)alkynyl which may have lower alkoxy(lower)alkyl;

morpholinyl(lower)alkynyl which may have 1 or 2

substituent(s) selected from the group consisting of ethyl, propyl, isopropyl, isobutyl,

35

spirocyclo(lower)alkyl, lower alkoxy(lower)alkyl,  
hydroxy(lower)alkyl, carboxy(lower)alkyl,  
di(lower alkyl)carbamoyl, lower alkoxycarbonyl and  
halo(lower)alkyl;

5 morpholinyl(lower)alkynyl which has methyl and  
lower alkoxy;

(dimethylmorpholino)(lower)alkynyl;

homomorpholinyl(lower)alkynyl which have halogen;

(morpholinylamino)propyl which may have lower  
10 alkanoyl;

thiomorpholinyl(lower)alkynyl which may have  
substituent(s);

homomorpholinylamino(lower)alkyl;

thiomorpholinylamino(lower)alkyl; or

15 saturated heterocyclicimino(lower)alkyl,

saturated heterocyclicaminocarbonyl(lower)alkyl or

saturated heterocyclic(lower)alkoxy(lower)alkyl,

each of which may have substituent(s),

provided that when

20  $R^4$  is 2-[N-methyl-N-(3-pyridylmethyl)amino]ethyl,

3-(3-pyridyl)propyl,

3-(3-pyridyl)-2-propynyl,

4-[(2-methoxymethyl)pyrrolidino]-2-butynyl,

4-thiomorpholino-2-butynyl,

25 3-(morpholinoamino)propyl,

4-morpholino-2-butenyl,

4-morpholino-2-butynyl, or

4-(3,3-dimethylmorpholino)-2-butynyl, then

$R^1$  is not 3,5-bis(trifluoromethyl)phenyl,

30 and a salt thereof.

2. The compound of claim 1, in which

Y is lower alkylene,

$R^1$  is  $C_6$ - $C_{10}$  aryl which may have 1 or 2 substituent(s)

35 selected from the group consisting of mono(or di

or tri)halo(lower)alkyl, halogen, lower alkylamino, di(lower)alkylamino and nitro,

$R^2$  is  $C_6-C_{10}$  aryl or indolyl, each of which may have 1 to 3 substituent(s) selected from the group consisting of lower alkyl, mono(or di or tri)halo(lower)alkyl, lower alkylenedioxy, hydroxy, hydroxy(lower)alkyl, lower alkoxy, lower alkylamino and di(lower)alkylamino,

$R^3$  is hydrogen, and

$R^4$  is pyridyl(lower)alkylamino(lower)alkynyl;

(2-pyridyl)propyl which may have 1 to 3 substituent(s) selected from the group consisting of lower alkyl, lower alkoxy, lower alkoxycarbonyl, mono(or di or tri)halo(lower)alkyl and halogen;

pyridyl, thiazolyl, imidazolyl or pyrazolyl, each of which may have 1 or 2 substituent(s) selected from the group consisting of lower alkyl, ar(lower)alkyl and pyridyl(lower)alkyl;

imidazolyl(lower)alkyl which has 1 or 2 substituent(s) selected from the group consisting of lower alkyl, lower alkynyl, ar(lower)alkyl, pyridyl(lower)alkyl, mono(or di or tri)halo(lower)alkyl and halogen;

(2-methyl-1H-imidazol-4-yl)(lower)alkyl which has 1 or 2 substituent(s) selected from the group consisting of isopropyl, lower alkynyl, ar(lower)alkyl, pyridyl(lower)alkyl, mono(or di or tri)halo(lower)alkyl and halogen;

(5-methyl-1H-imidazol-4-yl)(lower)alkyl which has 1 or 2 substituent(s) selected from the group consisting of isopropyl, lower alkynyl, ar(lower)alkyl, pyridyl(lower)alkyl, mono(or di or tri)halo(lower)alkyl and halogen;

piperidyl(lower)alkyl which may have hydroxy(lower)alkyl or lower alkoxy;

morpholinyl(lower)alkyl which has 1 or 2  
 substituent(s) selected from the group consisting  
 of ethyl, hydroxy(lower)alkyl, halo(lower)alkyl and  
 lower alkoxy(lower)alkyl;

5 morpholinyl(lower)alkyl which has lower alkyl and  
 lower alkoxy(lower)alkyl;  
 (3,5-dimethylmorpholino)(lower)alkyl;  
 morpholino(lower)alkenyl which may have lower alkyl  
 or lower alkoxy(lower)alkyl;

10 (2- or 3-morpholinyl)(lower)alkenyl which may have  
 lower alkoxycarbonyl;

pyrrolidinyl(lower)alkynyl which may have lower  
 alkoxy(lower)alkyl;

15 morpholinyl(lower)alkynyl which may have 1 or 2  
 substituent(s) selected from the group consisting  
 of ethyl, propyl, isopropyl, isobutyl,  
 spirocyclo(lower)alkyl, lower alkoxy(lower)alkyl,  
 hydroxy(lower)alkyl, carboxy(lower)alkyl, di(lower  
 alkyl)carbamoyl, lower alkoxycarbonyl and  
 20 halo(lower)alkyl;

morpholinyl(lower)alkynyl which has methyl and  
 lower alkoxy(lower)alkyl;

(dimethylmorpholino)(lower)alkynyl; or  
 homomorpholinyl(lower)alkynyl which may have  
 25 halogen.

3. The compound of claim 2, in which

Y is lower alkylene,

30  $R^1$  is phenyl which has 1 or 2 substituent(s) selected  
 from the group consisting of trihalo(lower)alkyl,  
 halogen, lower alkylamino, di(lower)alkylamino and  
 nitro,

$R^2$  is phenyl or indolyl, each of which have 1 or 2  
 substituent(s) selected from the group consisting  
 35 of lower alkyl, trihalo(lower)alkyl, lower

alkylenedioxy, hydroxy, hydroxy(lower)alkyl, lower alkoxy, lower alkylamino and di(lower)alkylamino,

R<sup>3</sup> is hydrogen, and

R<sup>4</sup> is (2-pyridyl)propyl which may have 1 to 3

substituent(s) selected from the group consisting of lower alkyl, lower alkoxy, mono(or di or tri)halo(lower)alkyl and halogen;

morpholinyl(lower)alkyl which has 1 or 2

substituent(s) selected from the group consisting of ethyl, hydroxy(lower)alkyl, halo(lower)alkyl and lower alkoxy(lower)alkyl;

morpholinyl(lower)alkynyl which may have 1 or 2

substituent(s) selected from the group consisting of ethyl, propyl, isopropyl, isobutyl,

spirocyclo(lower)alkyl, lower alkoxy(lower)alkyl, hydroxy(lower)alkyl, carboxy(lower)alkyl, di(lower alkyl)carbamoyl, lower alkoxycarbonyl and halo(lower)alkyl.

4. A compound of claim 3, which is selected from the group consisting of

(1) (2R)-1-[3,5-Bis(trifluoromethyl)benzoyl]-4-[4-((3S)-3-ethylmorpholino)-2-butynyl]-2-[(1H-indol-3-yl)methyl]piperazine,

(2) (2R)-1-[3,5-Bis(trifluoromethyl)benzoyl]-2-(3,4-dimethylbenzyl)-4-[2-((2S)-2-methoxymethyl-morpholino)ethyl]piperazine,

(3) (2R)-1-[3,5-Bis(trifluoromethyl)benzoyl]-2-(3,4-dimethylbenzyl)-4-[2-((3R)-3-methoxymethyl-morpholino)ethyl]piperazine,

(4) (2R)-1-[3,5-Bis(trifluoromethyl)benzoyl]-2-(3,4-dimethylbenzyl)-4-[2-((2R)-2-methoxymethyl-morpholino)ethyl]piperazine,

(5) (2R)-1-[3,5-Bis(trifluoromethyl)benzoyl]-2-[(1H-indol-3-yl)methyl]-4-[2-((2S)-2-methoxymethyl-

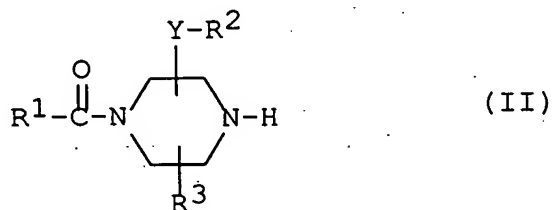
morpholino)ethyl]piperazine, and

(6) (2R)-1-[3,5-Bis(trifluoromethyl)benzoyl]-4-[2-  
((3R)-3-ethylmorpholino)ethyl]-2-[(1H-indol-3-yl)-  
methyl]piperazine

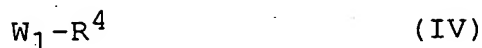
or a pharmaceutically acceptable salt thereof.

5. A process for the preparation of the compound of claim 1  
or a salt thereof, which comprises,

(1) reacting a compound of the formula (II) :

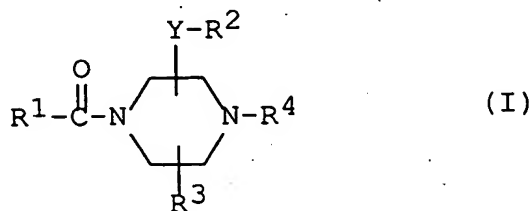


wherein  $R^1$ ,  $R^2$ ,  $R^3$  and Y are each as defined in claim 1,  
or a salt thereof, with a compound of the formula  
(III) :



wherein  $R^4$  is as defined in claim 1 and

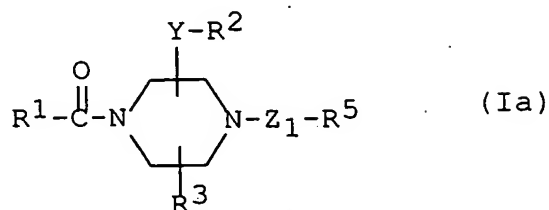
$W_1$  is a leaving group,  
or a salt thereof to give a compound of the formula  
(I) :



wherein  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^4$  and Y are each as defined in

claim 1, or a salt thereof,

(2) subjecting a compound of the formula (Ia) :



wherein  $\text{R}^1$ ,  $\text{R}^2$ ,  $\text{R}^3$  and Y are each as defined above,

$\text{R}^5$  is 2-pyridyl which may have 1 to 3

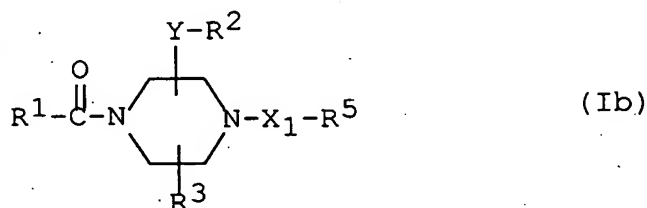
substituent(s) selected from the group  
consisting of lower alkyl, lower alkoxy,

lower alkoxycarbonyl, mono(or di or  
tri)halo(lower)alkyl and halogen; or

3-pyridyl which may have lower alkoxy or  
amino, and

$\text{Z}_1$  is lower alkynylene,

or a salt thereof to a reduction reaction to give a  
compound of the formula (Ib) :



wherein  $\text{R}^1$ ,  $\text{R}^2$ ,  $\text{R}^3$ , Y and  $\text{R}^5$  are each as defined above,

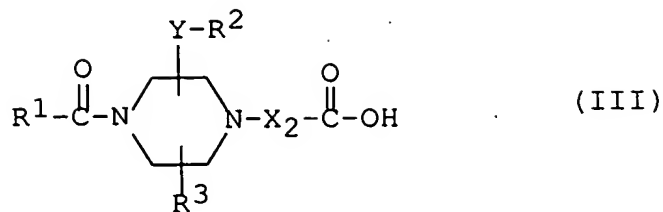
and

$\text{X}_1$  is lower alkylene,

or a salt thereof,

(3) reacting a compound of the formula (III) :



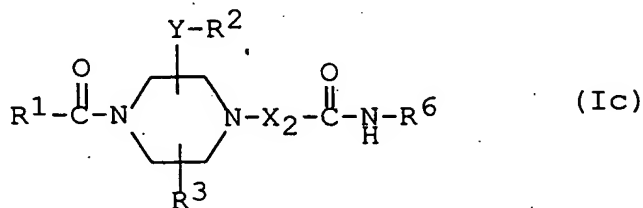


wherein  $\text{R}^1$ ,  $\text{R}^2$ ,  $\text{R}^3$  and Y are each as defined above,  
and

$\text{X}_2$  is lower alkylene,  
or its reactive derivative at the carboxy group or a  
salt thereof with a compound of the formula (V) :

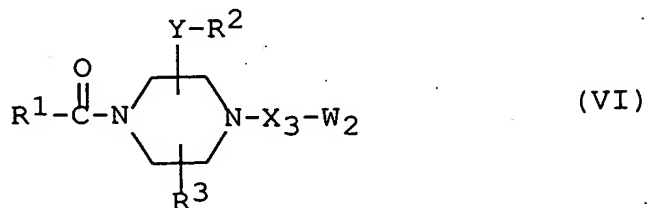


wherein  $\text{R}^6$  is saturated heterocyclic which may have  
substituent(s),  
or a salt thereof to give a compound (Ic) :



wherein  $\text{R}^1$ ,  $\text{R}^2$ ,  $\text{R}^3$ ,  $\text{R}^6$ ,  $\text{X}_2$  and Y are each as defined  
above,

(4) reacting a compound of the formula (VI) :



wherein  $R^1$ ,  $R^2$ ,  $R^3$  and Y are each as defined above,

$X_3$  is lower alkylene and

$W_2$  is a leaving group,

or a salt thereof with a compound of the formula

5 (VII) :



wherein  $R^7$  is pyridyl(lower)alkylamino;

N-(lower alkyl)-N-[pyridyl(lower)alkyl]-  
amino;

10 1-imidazolyl which may have 1 or 2  
substituent(s) selected from the group  
consisting of lower alkyl, lower alkynyl,  
ar(lower)alkyl, pyridyl(lower)alkyl,  
mono(or di or tri)halo(lower)alkyl and  
15 halogen;

1-pyrazolyl which may have  
hydroxy(lower)alkyl, carboxy(lower)alkyl,  
lower alkoxy carbonyl(lower)alkyl,  
morpholinyl(lower)alkyl or  
20 morpholinyl carbonyl(lower)alkyl;

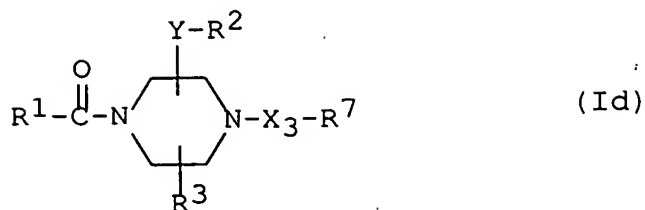
piperidino which may have  
hydroxy(lower)alkyl or lower alkoxy;  
morpholino which has 1 or 2  
substituent(s) selected from the group  
25 consisting of ethyl, hydroxy(lower)alkyl,  
halo(lower)alkyl and lower alkoxy-  
(lower)alkyl;

morpholino which has lower alkyl and  
lower alkoxy(lower)alkyl;  
30 3,5-dimethylmorpholino;  
morpholinylamino which may have lower  
alkanoyl;

homomorpholinylamino; or  
thiomorpholinylamino,

35 or a salt thereof to give a compound of the formula

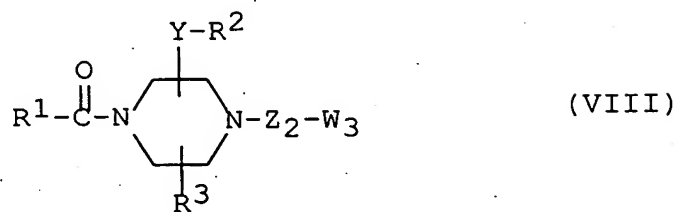
(Id) :



wherein  $\text{R}^1$ ,  $\text{R}^2$ ,  $\text{R}^3$ ,  $\text{R}^7$ ,  $\text{X}_3$  and  $\text{Y}$  are each as defined above,

or a salt thereof,

(5) reacting a compound of the formula (VIII) :



wherein  $\text{R}^1$ ,  $\text{R}^2$ ,  $\text{R}^3$  and  $\text{Y}$  are each as defined above,  
 $\text{Z}_2$  is lower alkenylene, and

$\text{W}_3$  is a leaving group,

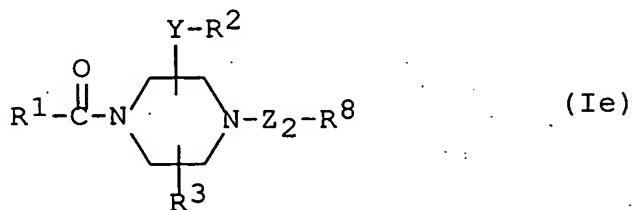
or a salt thereof with a compound of the formula (IX) :



wherein  $\text{R}^8$  is morpholino which may have lower alkyl or lower alkoxy(lower)alkyl,

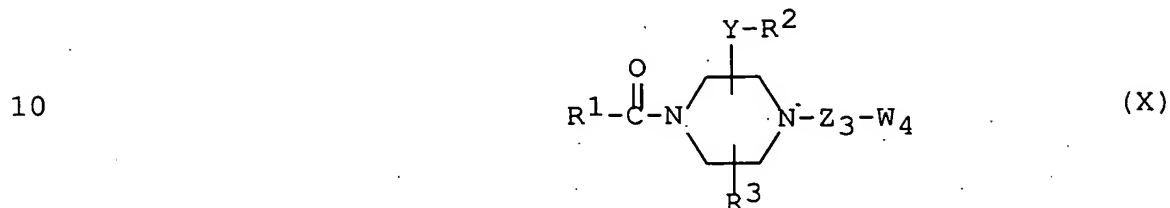
or a salt thereof to give a compound of the formula

(Ie) :



wherein  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^8$ , Y and  $Z_2$  are as defined as  
above,  
or a salt thereof,

5 (6) reacting compound of the formula (X) :

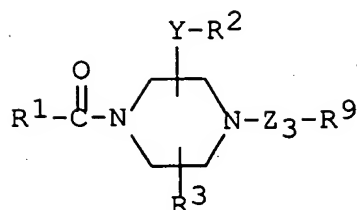


15 wherein  $R^1$ ,  $R^2$ ,  $R^3$  and Y are each as defined above,  
 $Z_3$  is a lower alkynylene and  
 $W_4$  is a leaving group,  
or a salt thereof with a compound of the formula (XI) :



wherein  $R^9$  is pyrrolidino which may have lower  
alkoxy(lower)alkyl;  
morpholino which may have 1 or 2  
substituent(s) selected from the group  
25 consisting of ethyl, propyl, isopropyl,  
isobutyl, spirocyclo(lower)alkyl, lower  
alkoxy(lower)alkyl, hydroxy(lower)alkyl,  
carboxy(lower)alkyl, di(lower  
alkyl)carbamoyl, lower alkoxy carbonyl and  
30 halo(lower)alkyl;  
morpholino which has methyl and lower  
alkoxy;  
dimethylmorpholino; or  
homomorpholino which has halogen,  
35 or a salt thereof to give a compound of the formula

(If) :



(If)

wherein  $\text{R}^1$ ,  $\text{R}^2$ ,  $\text{R}^3$ ,  $\text{R}^9$ , Y and  $\text{Z}_3$  are each as defined  
 above,  
 or a salt thereof.

6. A pharmaceutical composition which comprises, as an active ingredient, a compound of claim 1 or a pharmaceutically acceptable salt thereof in admixture with pharmaceutically acceptable carriers.
7. A compound of claim 1 for use as a medicament.
8. A method for treating or preventing Tachykinin-mediated diseases which comprises administering an effective amount of a compound of claim 1 or a pharmaceutically acceptable salt thereof to human being or animals.
9. A compound of claim 1 for use as Tachykinin antagonist.
10. Use of a compound of claim 1 for manufacture of a medicament for treating or preventing Tachykinin-mediated diseases.